According to still further features in the described preferred embodiments the composition is suitable for parenteral administration to a human.

The present invention successfully addresses the shortcomings of the presently known configurations by providing new horizons to the treatment of the devastating autoimmune disease multiple sclerosis.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention herein described, by way of example only, with reference to the accompanying drawings, wherein:

FIGs. 1A-F demonstrate IGIF mRNA in the inflamed EAE brain. Figures 1A, C, G and E - Rats were injected with 10^7 cells form L68-86 immunized rats to allow for the development of transferred EAE. Before adoptive transfer of disease (day 0), and at various time points: before the onset of disease (day 3), at the day of onset (day 5), the peak (day 7), following recovery (day 10), and 10 days after recovery (day 20) mid-brain and brain stem samples from six different rats at each time point were examined. mRNA was isolated from each sample and subjected to RT-PCR analysis using specific oligonucleotide primers constructed for IGIF (Figure 1C) and for IFN-γ (Figure 1E). Each amplification was calibrated to β-actin (Figure 1G) and verified by Southern Blot analysis. Southern bolt images were objectively assessed using an FujiFilm Thermal System. Figures 1B, D, F and H - Rats were immunized with p68-86/CFA and developed active EAE. Before the induction of disease (day 0), and at various time points: before the onset of disease (day 8), at the peak (day 13), and following recovery (day 21) mid-brain and brain stem samples from six different rats at each time point were examined for mRNA transcription for IGIF (Figure 1D) and IFN-γ (Figure 1F) and calibrated to β-actin (Figure 1H), as described above.

FIGs. 2A-D demonstrate that neutralizing antibodies to recombinant rat IGIF block IFN-γ production in cultured T cells. Spleen cells from naive (Figures 2A and 2B) or from p68-86/CFA primed (day 9) Lewis rats (Figures 2C and 2D) were cultured *in vitro* with either Con A (Figures 2A and 2B), or with 100 μM of MBP p68-86 (Figures 2C and 2D) with or without the addition of 100 ng/ml of rabbit anti-rat IGIF (IgG) neutralizing antibodies (Figures 2A and 2C) or with IgG from non-immunized rabbits (data not shown), with or without the addition of 400 ng/ml recombinant rat IGIF (Figures 2B and 2D). After 72 hours of stimulation IFN-γ levels were

determined in the culture supernatants by an ELISA assay. Results are the mean ± S.E. of triplicate cultures.

FIGs. 3A-B demonstrate that neutralizing antibodies to recombinant rat IGIF block the development of both active and transferred EAE. Figure 3A - Lewis rats were immunized with p68-86/CFA to induce active EAE and then separated into three groups of six rats each. Eight, ten and eleven days after induction of disease, these groups were injected IV with rabbit anti-rat IGIF (IgG fraction 100μg/rat), with IgG fraction purified from non-immunized rabbits (control IgG), or with PBS. The rats were then monitored daily for clinical signs of EAE by an observer blind to the treatment protocol. Results are presented as mean clinical score ± S.E. Figure 3B - Transferred EAE was induced as described above (Figure 1). Recipients were then separated into three groups of six rats each. Three, five and seven days after induction of disease these groups were injected as described above (Figure 3A) and monitored daily for clinical signs of EAE by an observer blind to the treatment protocol. Results are presented as mean clinical score ± S.E.

FIGs. 4A-D demonstrate alteration in IFN-γ and IL-4 production in EAE rats injected with anti-IGIF neutralizing antibodies. Lewis rats were immunized with p68-86/CFA to induce active EAE and separated into three groups. Five and seven days after disease induction these groups were injected IV with either rabbit anti-rat IGIF (IgG fraction 100 μg/rat), with purified IgG from non-immunized rabbits, or with PBS. Before the onset of disease (day 9) splenic T cells from three rats in each group were cultured with 100 μM MBP p68-86 for 72 hours in stimulation medium that was not (Figures 4A and 4B) or was (Figures 4C and 4D) supplemented with recombinant rat IL-4 (5 ng/ml). After 72 hours of stimulation, IFN-γ levels were determined in culture supernatants by an ELISA assay. Results are of triplicate cultures expressed as mean ± S.E.

FIG. 5 demonstrates alteration in TNF-α production in EAE rats injected with anti-IGIF neutralizing antibodies. Levels of TNF-α were determined in supernatants obtained in experiment described in Figures 4A and 4B, by an ELISA assay. Results are of triplicate cultures expressed as mean ± S.E.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is of interferon gamma inducing factor (IGIF) based vaccines which can be used in the treatment of multiple sclerosis. Specifically, the present invention can be used to confer protective immunity against multiple sclerosis.

The principles and operation of the interferon gamma inducing factor (IGIF) based vaccines according to the present invention may be better understood with reference to the drawings and accompanying descriptions.

Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

In autoimmune conditions, T cells reactive to self-antigens escape elimination in the thymus, and are activated in the periphery where they can provoke damage to specific cells and organs. Perturbation of the balance between self-reactive T cells with different cytokine profiles may serve as an effective way of restraining the harmful effect of autoimmune T cells (12, 14-16, 20-22, 38, 41-43).

Cytokines present at the initiation of $CD4^+$ T cell responses determine whether a Th1 or a Th2 response will predominate (1-6). Thus, administration of IL-4 or of antibodies to IL-12 preferentially favors Th2 selection *in vivo* and thus serves as a powerful way to inhibit two different T cell mediated autoimmune diseases: EAE and IDDM (12, 15, 22)

It is well known that high levels of IFN-γ positively select for TNF-α secreting Th1 cells (6). A previous study showed that administration of anti-IL-12 neutralizing antibodies blocks EAE while inducing a marked reduction of both IFN-γ and TNF-α production (15). IFN-γ and TNF-α together then exhibit a synergistic effect on enhancing expression of adhesion molecules on endothelial cells (44), and on eliciting the inflammatory process, which can be reversed by either anti-adhesion molecule immunotherapy (45, 46), or by blocking TNF-α (44, 47-50). It was previously demonstrated that EAE resistance acquired by soluble antigen therapy can be reversed by anti-IL-4 neutralizing antibodies (38).